

ACC CVS database

Beginners user guide

From its earliest days, the database has been set up to answer the following question: 'I have got these cytogenetic results from direct preparations and cultured cells from a CVS, what does this mean in terms of the fetal karyotype?' It is still set up this way. If you remember this question, you are most of the way towards understanding how this version works!

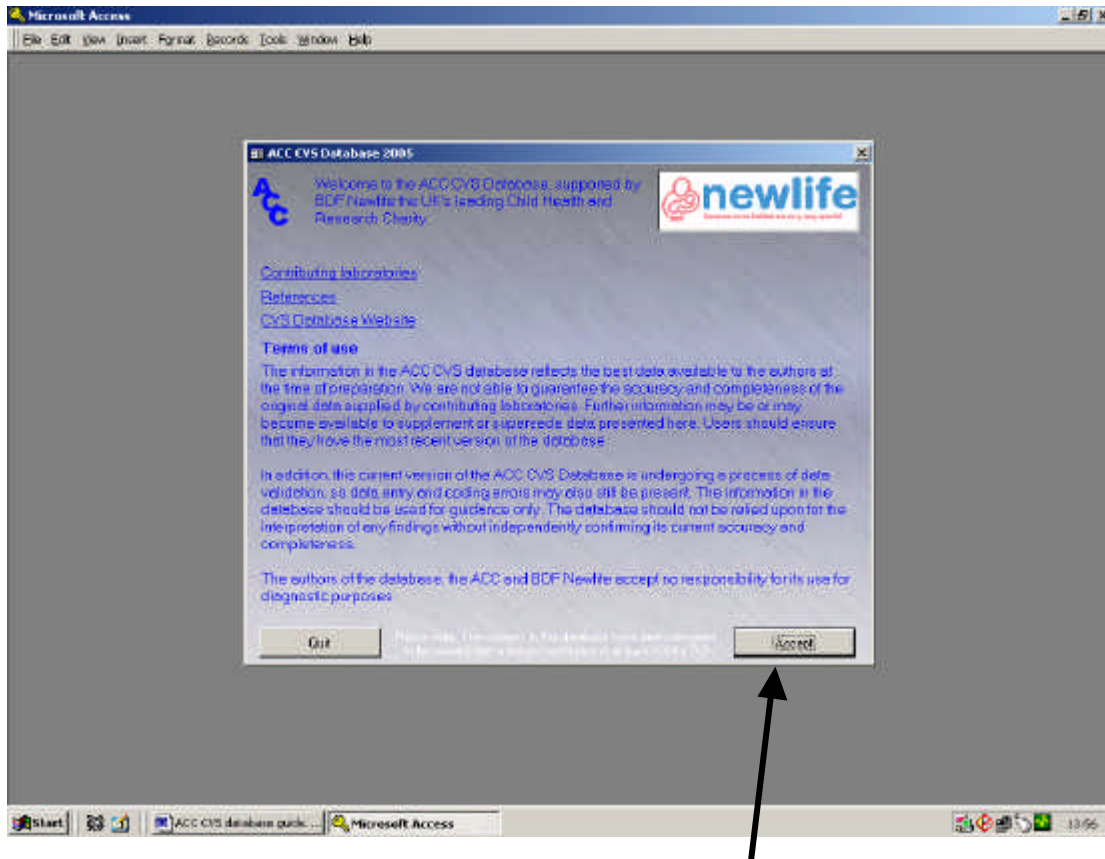
This guide shows you how to move around the database and how to do simple searches. The bits in **bold** tell you what to do. The bits in 'ordinary text' are key bits of information to help you understand what you are doing. The bits in *italics* are additional information you may find useful, but you can probably skip these initially!

Enter the database.

Although the database contains information on IUGR, UPD etc., in CVS, and it is possible to use the database to look at these, current searches are not set up with this in mind. The database organisers can probably help with such analyses, if you contact them directly.

This first electronic version of the database essentially mirrored earlier paper versions. This new version incorporates a much more sophisticated coding and searching capacity, which you will probably remain completely unaware of! This enables any case to have any number of independent codings associated with it, so that cases with complex karyotypes and/or multiple cytogenetic abnormalities will appear in their correct place in each relevant search. It also now includes complete coding of case outcome, also searchable. The user can see, but not alter, this coding, so that if they wish they can better understand how the searches work.

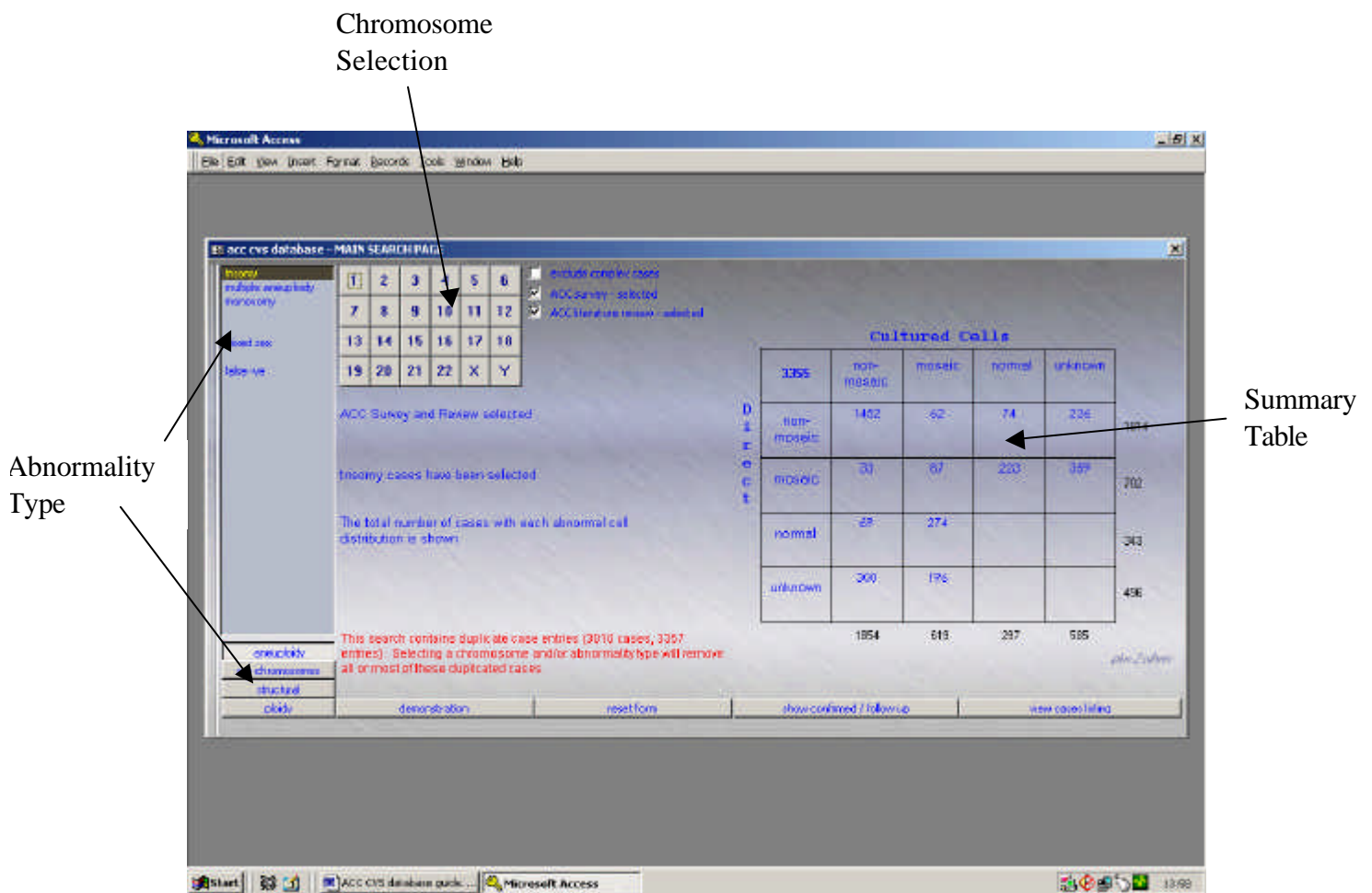
A new innovation is that a Summary Table on the Main Search Page displays either the total number of selected cases or a summary of case outcome, enabling the user to know when they have a manageable number of cases for subsequent full display. The Summary Table is also useful for data analysis.



This is the initial page you will see. **Read and click on Accept.**

You can also get to a list of laboratories that contributed to the ACC database and a list of publications used for the literature review as well as a direct link to the database website if you are online. The latter means you don't have to remember the website address for future downloads.

Tip: If you are online, you can get directly to the PubMed abstract, by clicking on individual references in the literature listing. You should also be able to access full articles if you have the appropriate subscriptions in place.

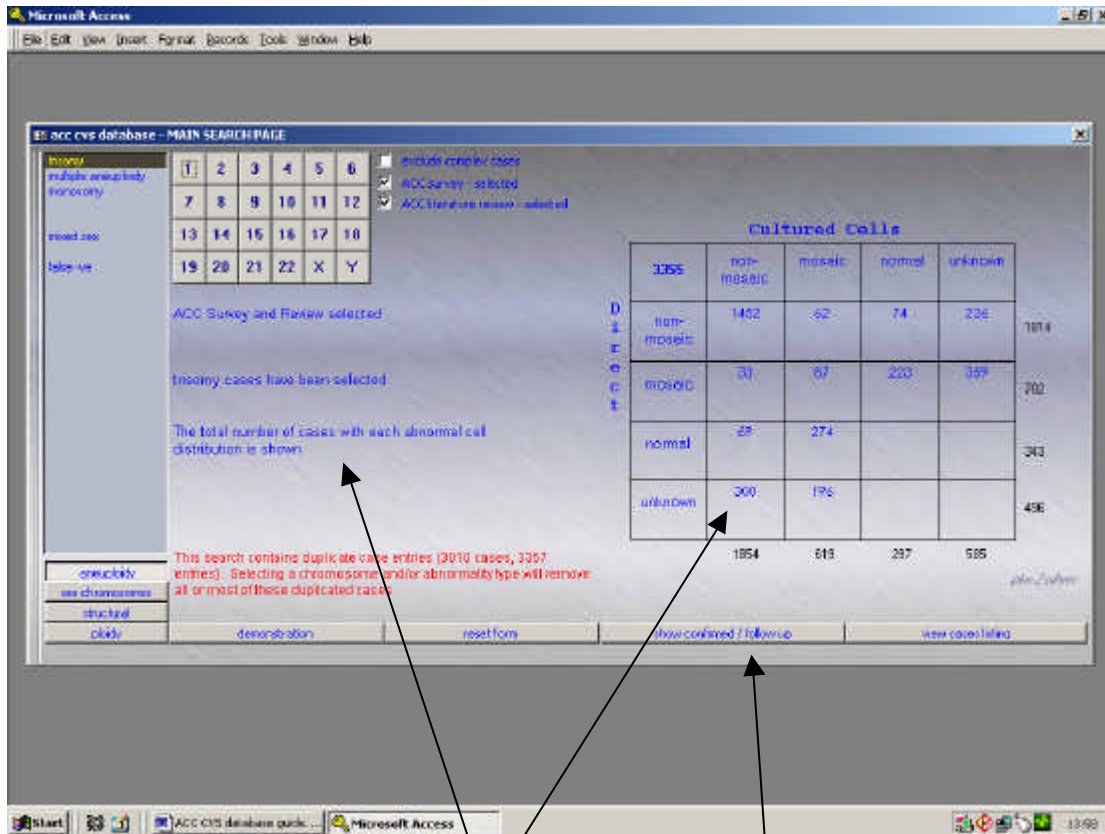


This is the Main Search Page, On the left you get the Abnormality Type menu, next to it, you get the Chromosome Selection menu and on the right you get a Summary Table showing how many cases you have in each category of abnormal cell distribution for any selected abnormality and chromosome combination. The Summary Table is a grid with the direct and culture results for any search by Abnormality and Chromosome, categorised as non-mosaic abnormal, mosaic abnormal, normal or unknown. You will also find a helpful block of text in the middle of the page. This details your current search, in case you lose track of where you are! The use of other options on the Main Search Page is described later.

The default setting is 'trisomy' for the Abnormality Type and searching the whole database (both ACC cases and literature cases). No chromosome is specified. The top left corner of the Summary Table gives the total number of cases of trisomy, the grid gives the number of cases in each category of abnormal cell distribution. Totals for rows and columns also appear. Combinations consisting of only normal and unknown are blank, as they are invalid. The Summary Table also gives you access to Case Listings for entries with abnormal cell distributions in any single part or combination of parts of the grid.

An 'exclude complex cases' option is available for searching trisomies and some other abnormalities. It will disappear in searches where it is counter-productive. If you select this, it will exclude multiple trisomies and things like trisomies derived from 3:1 segregations, which are probably of little interest in standard searches.

Try putting 'exclude complex cases' on and off.



The figures you are seeing in the grid are the total number of cases for the abnormality type/chromosome abnormality that has been selected; this view is termed 'show all cases'. If you click on the 'show confirmed/follow up' bit of the bottom bar, you select cases with useful follow-up of the cytogenetic abnormality in the fetus.

Try clicking on 'show confirmed/ follow-up'

NB When you do non-specific searches like 'trisomy' without selecting a chromosome, the coding of double trisomies etc. can give multiple entries in the Summary Table (see text in red). This also occurs with other non-specific searches. Multiple entries are a consequence of the coding we have used to deal with complex cases and they usually go away when you do a more detailed search.

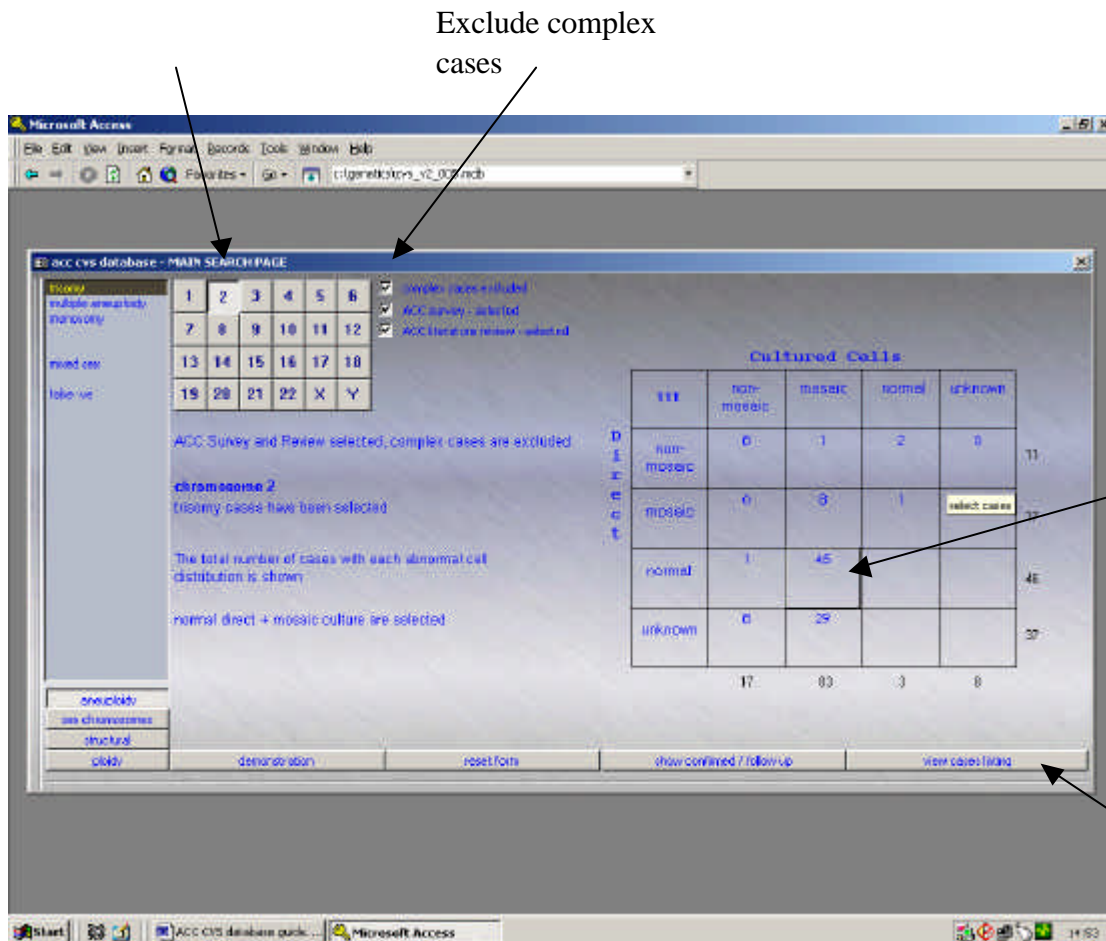
The screenshot shows a Microsoft Access window titled "acc cvs database - MAIN SEARCH PAGE". On the left, there is a search grid with columns 1-6 and rows for chromosomes 1-22, X, and Y. Below the grid, there are checkboxes for "exclude complex cases", "ACC survey - selected", and "ACC literature review - selected". A "Cultured Cells" table is displayed on the right, showing counts for different cell types. At the bottom, there are buttons for "denotation", "reset form", "show all cases", and "view cases listed". A red warning message states: "This search contains duplicate case entries (3010 cases, 3257 entries). Selecting a chromosome and/or abnormality type will remove all or most of these duplicated cases." Arrows from the text below point to the "show all cases" button and the "Cultured Cells" table.

| | not-mosaic | mosaic | normal | unknown | |
|------------|------------|--------|--------|---------|-----|
| non-mosaic | 627/692 | 7/46 | 1/49 | 97/154 | 940 |
| mosaic | 18/19 | 14/47 | 2/112 | 26/334 | 512 |
| normal | 42/49 | 20/166 | | | 215 |
| unknown | 14/137 | 13/130 | | | 267 |
| | 667 | 388 | 161 | 498 | |

The fraction you now see is the number of cases with the cytogenetic abnormality confirmed in the fetus, divided by the total number of cases with useful fetal cytogenetic follow-up. Also included, are a small number where the scan or post-mortem information is considered sufficient to confirm or refute the prenatal cytogenetic findings. You can see how these are coded later. You can go back to the original view using 'show all cases'.

Try moving between 'all' and 'confirmed' views.

Looking at all trisomies at once is probably of limited value!



Select 'exclude complex cases' and select chromosome 2. You will see the numbers of cases in the Summary Table fall to manageable proportions (see above). The default is 'show all cases'. Try moving between the 'show all cases' and 'show confirmed cases/follow-up' options again.

By single-clicking on any part of the grid, you can then select any combination of cell distributions from the Summary Table. This works in either 'show all cases' or 'show confirmed/follow up' options. Then click the 'view Case Listings' option on the bottom bar, to get a list of the cases with the selected cell distributions. This also works with total numbers of cases (top left of grid). You can simultaneously select two or more abnormal cell distributions, and you can select/deselect any number of them with single clicks, until you get the combination you want. You can also select rows and columns by clicking on the non-mosaic, mosaic headings. The text tells you what you have selected.

Click on normal directs and mosaic culture (45 cases) and then 'View cases listing', to see the Case Listing.

Microsoft Access

File Edit View Insert Format Records Tools Window Help

acc cvs database - CASES LISTING

45 entries
45 cases

45 entries have been selected
cases with mixed direct + mixed culture are shown

| Origin | ID | Direct | %Direct | Culture | %Culture | Confirmation | Interpretation |
|--------|----------|--------|---------|---------------|----------|--------------|----------------|
| ACC | 100492 | 46,XX | 0% | 47,XX+2/46,XX | 28% | no follow up | Not known |
| ACC | 327289 | 46,XX | 0% | 47,XX+2/46,XX | 7% | no follow up | Not known |
| ACC | 870049 | 46,XX | 0% | 47,XX+2/46,XX | 30% | no follow up | Not known |
| ACC | 870266 | 46,XX | 0% | 47,XX+2/46,XX | 52% | no follow up | Not known |
| ACC | 890426 | 46,XY | 0% | 47,XY+2/46,XY | 64% | no (cyto) | CFM |
| ACC | 895790 | 46,XX | 0% | 47,XX+2/46,XX | 52% | no follow up | Not known |
| ACC | 9217000 | 46,XY | 0% | 47,XY+2/46,XY | 56% | no follow up | Not known |
| ACC | 930400 | 46,XX | 0% | 47,XX+2/46,XX | 4% | no follow up | Not known |
| ACC | 9504027 | 46,XX | 0% | 47,XX+2/46,XX | 22% | no follow up | Not known |
| ACC | 971803 | 46,XX | 0% | 47,XX+2/46,XX | 47% | no follow up | Not known |
| ACC | C802368 | 46,XY | 0% | 47,XY+2/46,XY | 60% | no (cyto) | CFM |
| ACC | C83120 | 46,XY | 0% | 47,XY+2/46,XY | 38% | no follow up | Not known |
| ACC | C836049 | 46,XY | 0% | 47,XY+2/46,XY | 6% | no follow up | Not known |
| ACC | C850012 | 46,XY | 0% | 47,XY+2/46,XY | - | no follow up | Not known |
| ACC | C860372 | 46,XX | 0% | 47,XX+2/46,XX | 43% | no (cyto) | CFM |
| ACC | C86714 | 46,XY | 0% | 47,XY+2/46,XY | 30% | no follow up | Not known |
| ACC | C8670 | 46,XY | 0% | 47,XY+2/46,XY | 7% | no follow up | Not known |
| ACC | C873214 | 46,XX | 0% | 47,XX+2/46,XX | 50% | no follow up | Not known |
| ACC | C870020 | 46,XY | 0% | 47,XY+2/46,XY | 57% | no follow up | Not known |
| ACC | C801353 | 46,XY | 0% | 47,XY+2/46,XY | 20% | no (cyto) | CFM |
| ACC | C8973 | 46,XY | 0% | 47,XY+2/46,XY | 30% | no follow up | Not known |
| ACC | Cy003797 | 46,XY | 0% | 47,XY+2/46,XY | 65% | no (cyto) | CFM |
| ACC | Cy004897 | 46,XX | 0% | 47,XX+2/46,XX | - | no follow up | Not known |

show duplicate select all view selected cases

You should now see the Case Listings page, showing basic information about the 45 cases you have selected. The default order is alphanumeric based on laboratory/literature case of origin.

If you click on 'Select all' then 'View selected cases' you will move to detailed Case Entries of all 45 cases – useful when you want the lot, particularly when numbers are small.

Microsoft Access

File Edit View Insert Format Records Tools Window Help

acc cvs database - CASES LISTING

45 entries
45 cases

Warning: Some fields have been selected.
Cases with normal direct + normal culture are shown

| Origin | ID | Direct | %Direct | Culture | %Culture | Continuation | Interpretation |
|--------|----------|--------|---------|---------------|----------|--------------|----------------|
| ACC | 100482 | 46,XX | 0% | 47,XX+2/46,XX | 28% | no follow up | Not known |
| ACC | 327289 | 46,XX | 0% | 47,XX+2/46,XX | 7% | no follow up | Not known |
| ACC | 877049 | 46,XX | 0% | 47,XX+2/46,XX | 30% | no follow up | Not known |
| ACC | 877266 | 46,XX | 0% | 47,XX+2/46,XX | 52% | no follow up | Not known |
| ACC | 890426 | 46,XY | 0% | 47,XY+2/46,XY | 64% | no (cyto) | CPM |
| ACC | 895720 | 46,XX | 0% | 47,XX+2/46,XX | 52% | no follow up | Not known |
| ACC | 8217600 | 46,XY | 0% | 47,XY+2/46,XY | 56% | no follow up | Not known |
| ACC | 832406 | 46,XX | 0% | 47,XX+2/46,XX | 4% | no follow up | Not known |
| ACC | 9504627 | 46,XX | 0% | 47,XX+2/46,XX | 22% | no follow up | Not known |
| ACC | 971903 | 46,XX | 0% | 47,XX+2/46,XX | 47% | no follow up | Not known |
| ACC | C802360 | 46,XY | 0% | 47,XY+2/46,XY | 68% | no (cyto) | CPM |
| ACC | C83120 | 46,XY | 0% | 47,XY+2/46,XY | 38% | no follow up | Not known |
| ACC | C835049 | 46,XY | 0% | 47,XY+2/46,XY | 5% | no follow up | Not known |
| ACC | C850012 | 46,XY | 0% | 47,XY+2/46,XY | - | no follow up | Not known |
| ACC | C860372 | 46,XX | 0% | 47,XX+2/46,XX | 43% | no (cyto) | CPM |
| ACC | C86714 | 46,XY | 0% | 47,XY+2/46,XY | 30% | no follow up | Not known |
| ACC | C8678 | 46,XY | 0% | 47,XY+2/46,XY | 7% | no follow up | Not known |
| ACC | C873214 | 46,XX | 0% | 47,XX+2/46,XX | 50% | no follow up | Not known |
| ACC | C873020 | 46,XY | 0% | 47,XY+2/46,XY | 57% | no follow up | Not known |
| ACC | C801353 | 46,XY | 0% | 47,XY+2/46,XY | 20% | no (cyto) | CPM |
| ACC | C8973 | 46,XY | 0% | 47,XY+2/46,XY | 30% | no follow up | Not known |
| ACC | Cy803797 | 46,XY | 0% | 47,XY+2/46,XY | 65% | no (cyto) | CPM |
| ACC | Cy104857 | 46,XX | 0% | 47,XX+2/46,XX | - | no follow up | Not known |

show duplicate select all view selected cases

You can also select individual cases or groups of cases to see in detail, if you want to do a more specific search. Single clicks will select individual cases. If you click and drag, you can select blocks of cases. Using Shift and click or Ctrl and click, you can select any combination of cases. Click and drag also works with Ctrl, and you can also 'select all' and de-select cases you don't want.

Try selecting different combinations of cases.

Microsoft Access

ACC CVS database - CASES LISTING

45 entries
45 cases

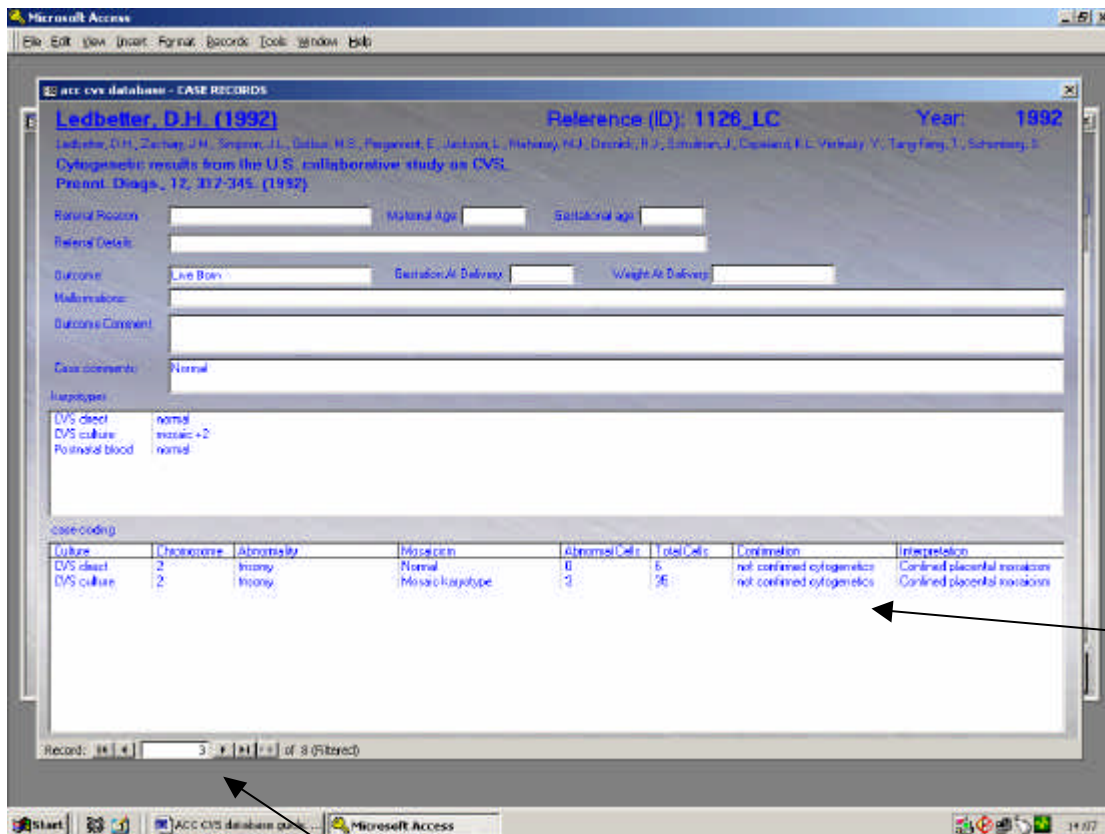
| Origin | ID | Direct | %Direct | Culture | %Culture | Confirmation | Interpretation |
|--------|-----------|--------|---------|------------------------|----------|--------------|----------------|
| LIT | 0346_LC | normal | 0% | mosaic +2 | - | no (cyto) | CFM |
| LIT | 0838_LC | 46,XY | 0% | 47,XY,+2(46,XX) | - | no (cyto) | CFM |
| LIT | 0940_LC | 46,XX | 0% | 47,XX,+2(46,XX) | - | no (cyto) | CFM |
| LIT | 0346_LC | normal | 0% | mosaic +2 | - | no (cyto) | CFM |
| ACC | C950012 | 46,XY | 0% | 47,XY,+2(46,XY) | - | no follow up | Not known |
| ACC | Cv0048/97 | 46,XX | 0% | 47,XX,+2(46,XX) | - | no follow up | Not known |
| ACC | 9302400 | 46,XX | 0% | 47,XX,+2(46,XX) | 4% | no follow up | Not known |
| LIT | 0352_LC | normal | 0% | mosaic +2 | 4% | no follow up | Not known |
| LIT | 0349_LC | normal | 0% | mosaic +2 | 4% | no follow up | Not known |
| ACC | C935049 | 46,XY | 0% | 47,XY,+2(46,XY) | 5% | no follow up | Not known |
| LIT | 0353_LC | normal | 0% | mosaic +2 | 7% | no follow up | Not known |
| ACC | 327289 | 46,XX | 0% | 47,XX,+2(46,XX) | 7% | no follow up | Not known |
| ACC | C9670 | 46,XY | 0% | 47,XY,+2(46,XY) | 7% | no follow up | Not known |
| LIT | 1120_LC | normal | 0% | mosaic +2 | 9% | no (cyto) | CFM |
| LIT | 0350_LC | normal | 0% | mosaic +2 | 11% | no follow up | Not known |
| LIT | 0348_LC | normal | 0% | mosaic +2 | 12% | no follow up | Not known |
| LIT | 0404_LC | normal | 0% | mosaic +2 | 12% | no follow up | Not known |
| LIT | 0976_LC | 46,XX | 0% | 47,XX,+2(7)(46,XX[+4]) | 13% | no follow up | Not known |
| LIT | 0330_LC | normal | 0% | mosaic +2 | 13% | no follow up | Not known |
| ACC | Cv100939 | 46,XX | 0% | 47,XX,+2(46,XX) | 18% | no follow up | Not known |
| ACC | C98-1153 | 46,XY | 0% | 47,XY,+2(46,XY) | 20% | no (cyto) | CFM |
| ACC | 9504027 | 46,XX | 0% | 47,XX,+2(46,XX) | 22% | no follow up | Not known |
| LIT | 0397_LC | normal | 0% | mosaic +2 | 23% | no (cyto) | CFM |

show duplicate select all view selected cases

We have incorporated a sorting feature on the Case Listings, which is designed to put groups of cases that you might want to co-select, in blocks next to each other. By clicking on any heading, you can toggle between alphanumeric sorting upwards and alphanumeric sorting downwards, for that column, and the default order. Although available on all headings, you may find this feature particularly helpful for stacking by % of abnormal cells (direct or culture), confirmation or interpretation. When a column sort is active, ? or ? will appear in the highlighted heading. Only one column sort can be active at any one time. The page above shows sorting by % of abnormal cells in cultures, followed by selection of a group of cases between 9% and 20%.

Try sorting and selecting cases using combinations of the above methods and then view the full Individual Case Entries for any multiple selection.

You might have already discovered that by double clicking on any individual case, you get taken directly to its full Individual Case Entry.

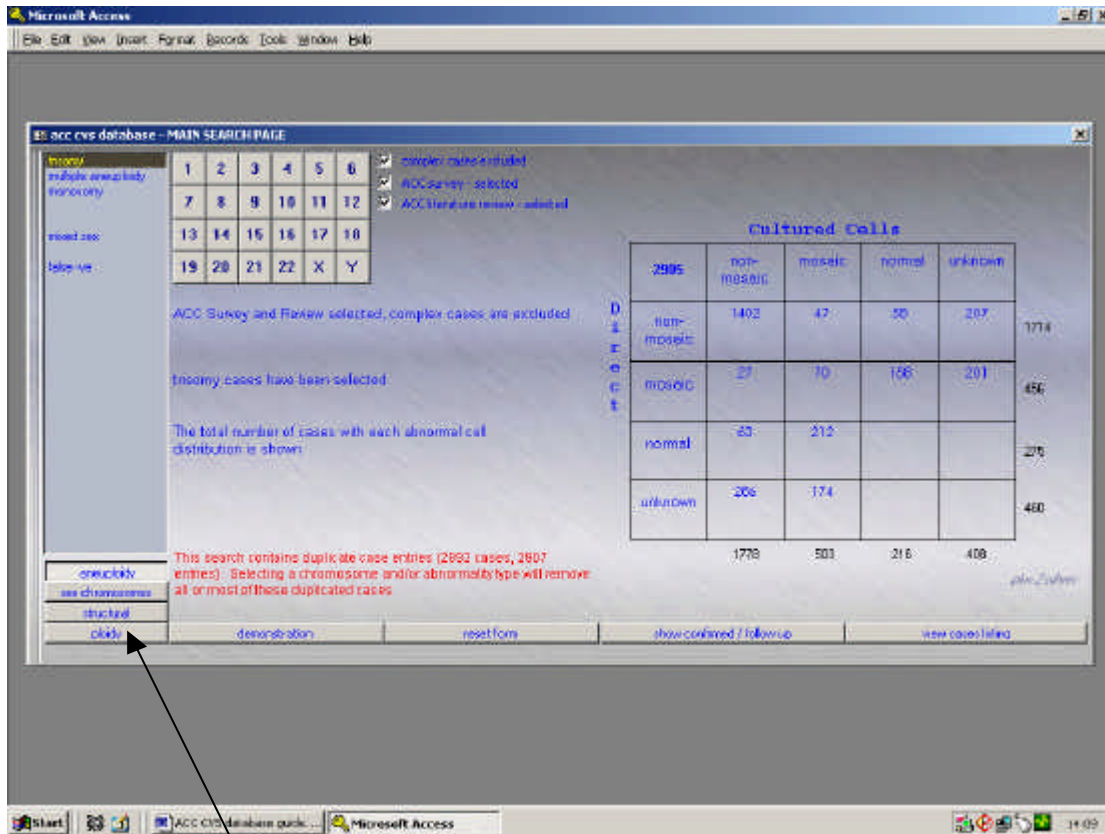


This takes you to the full Individual Case Entries, which will look like the above. You can move between cases using these buttons. Most of the data shown is fairly self-explanatory.

Check through a few Individual Case Entries to familiarise yourself with how they are laid out. Return to the Main Search Page, by closing the Individual Case Entry and Case Listings pages. Select another trisomy, and try a search on your own.

The lower part of the page shows the coding we have used. This area also contains the information on the total numbers of cells analysed and the number with the relevant abnormality, where available. For multiple cytogenetic abnormalities, this can get quite complicated, as both the 'affected' and 'total' can vary. These figures are used by the database to generate the %ages seen in the previous page. For this reason, some of these cell numbers you see are 'artificial' to cope with reports that simply say 'all cells' or '50% of cells' were affected. (These should eventually all appear with 1.0 as the total number of cells, and something like 0.5 as the number of abnormal cells, to make them obvious.) Where helpful, mainly for complex mosaic cases, the numbers of cells for each cell line also appear in the ISCN karyotypes.

Tip: If you click on the Laboratory name (top left) this will take you to details of the submitting laboratory. For literature cases, if you are online, clicking on the lead author's name will take you to the PubMed abstract. You will also have access to the full article, if you have the appropriate subscriptions in place.

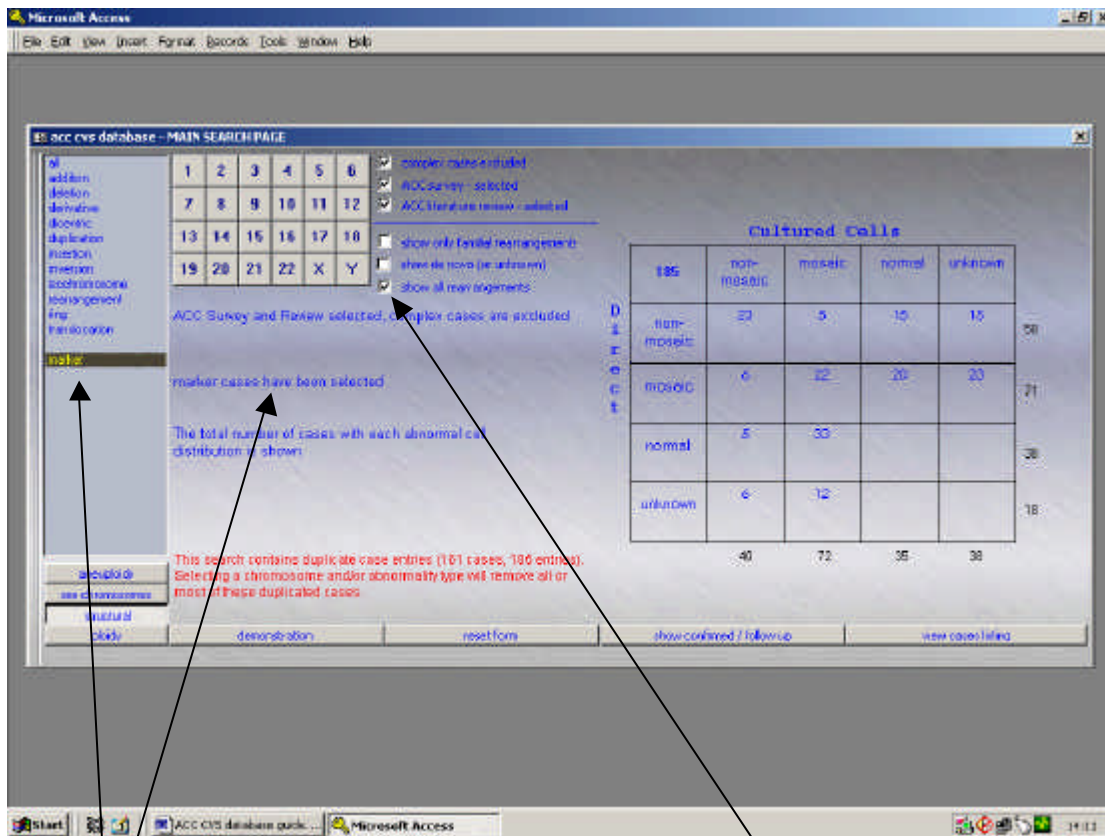


The default Abnormality Type menu can be used to select the other options displayed, such as 'multiple trisomies'. Selecting 'sex chromosomes', 'structural' or 'ploidy' below, will give further options.

Have a look at other options on the default Abnormality Type menu and the options on the other lists.

Some of the features on the main search screen may disappear, be replaced or become inactive, in a logical manner, as you do this (see following examples). This stops you doing inappropriate things, like trying to select chromosome 7 when you are searching within the sex chromosome abnormalities. It also offers features that are useful only for specific abnormality types.

Apart from this, all subsequent aspects of narrowing down searches are identical to the trisomies. Some examples/hints for other abnormalities follow.



Select marker chromosomes from the Structural Abnormality menu.

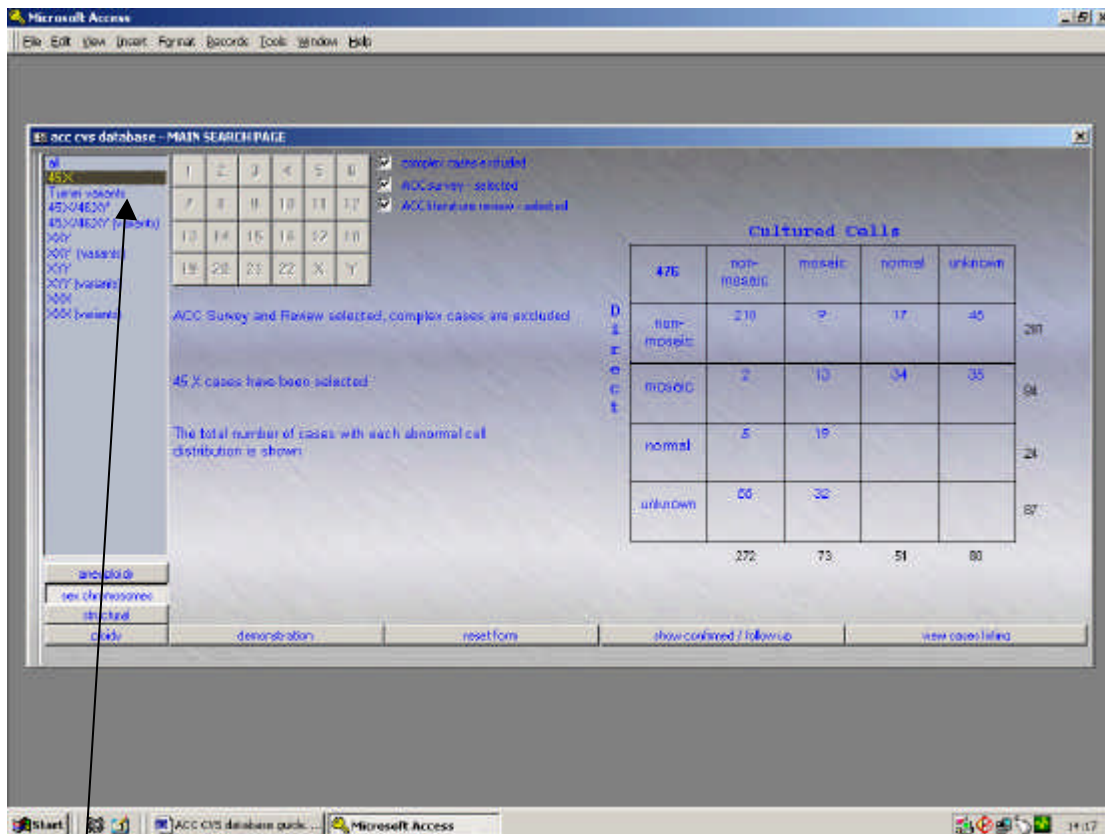
You should see the above. In this initial view, the Summary Table includes all marker chromosome cases. Using the 'exclude complex cases' option, you can get rid of multiple trisomies involving markers, if you want. You can also select for de novo or familial markers.

Some cases have details of the chromosomal origin of the marker. If you select an individual chromosome, you will get only those cases where this information is available. Cases where the marker is described as 'either 13 or 21 derived' appear as both 13 derived and 21 derived*.

Selecting cases from the Summary Table and Case Listings is the same as for trisomies.

Try doing a search on a marker, with and without selecting a chromosomal origin

**Be aware that this gives multiple entries in the Summary Table for non-specific searches (text in red).*



Select 'sex chromosomes' on the lower part of the Abnormality Type menu, to display the main categories of sex chromosome abnormalities. The default screen is 'all' sex chromosome abnormalities. The individual chromosome search is not valid and is disabled. 45,X has been selected in the above example.

For each of the main sex chromosome abnormalities, the Abnormality Type menu gives two mutually exclusive categories. For female 45,X cases, these are standard '45,X', where only 45,X and 46,XX lines were detected in the CVS, and 'variant Turner', which includes essentially everything else where other karyotypes, associated with Turner syndrome, are present in any combination. The same logic applies to the others. Cases such as X/XXX/XX mosaics are coded both as 'Turner variants' and 'XXX variants' so you can look in either category to find them.

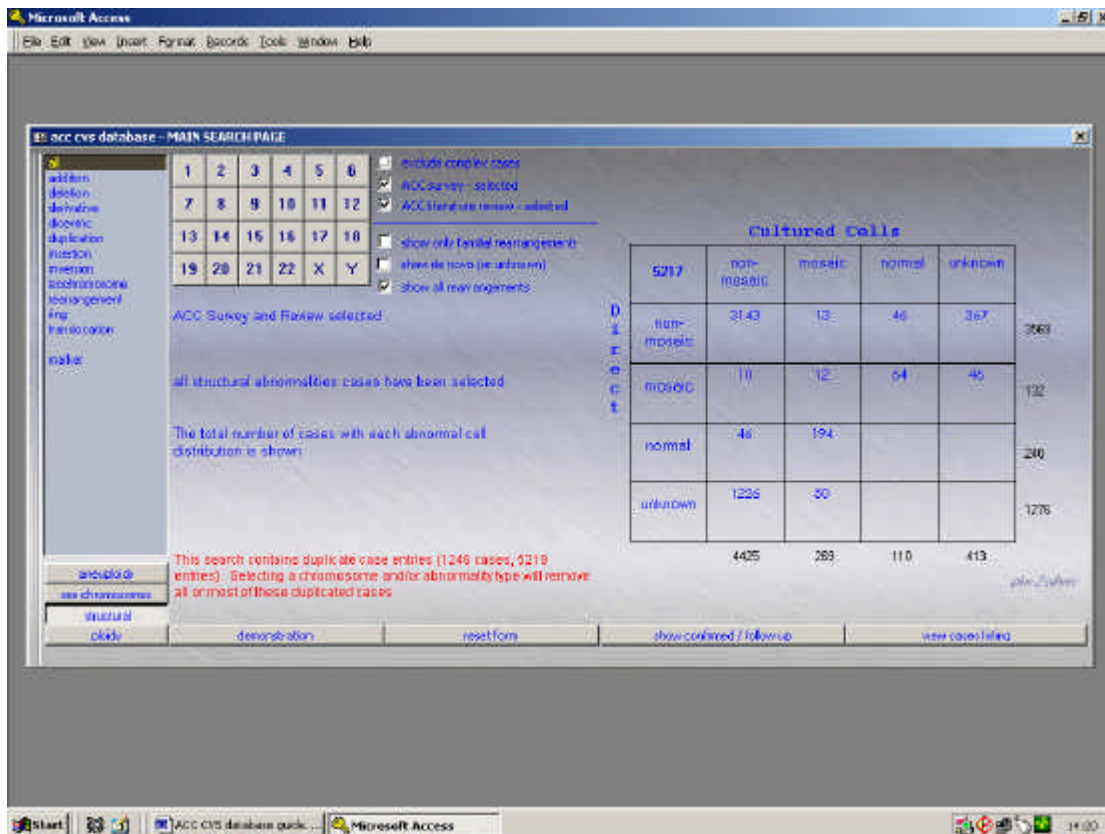
Select 45,X. Use the Summary Table to select an abnormal cell distribution. Subsequent searching is the same as for trisomies.

Repeat for Turner variants, to familiarise yourself with how the cases are categorised.

If you think about how cases are categorised, a case of 45,X/46,XX in direct preparations with no culture result, will be listed as '45,X'. The same direct result, but with 45,X/47,XXX/46,XX in the cultures, would be listed not as '45,X' but as a '45,X variant' and a '47,XXX variant'. The same logic applies to 45,X with either male or female outcomes. As coding is based on the initial findings in the CVS, it also means that a case of 45,X/46,XX in direct preparations and in cultured cells will appear in

the 45,X list, even if the fetus itself was subsequently found to have a variant Turner karyotype, such as one involving isoXq.

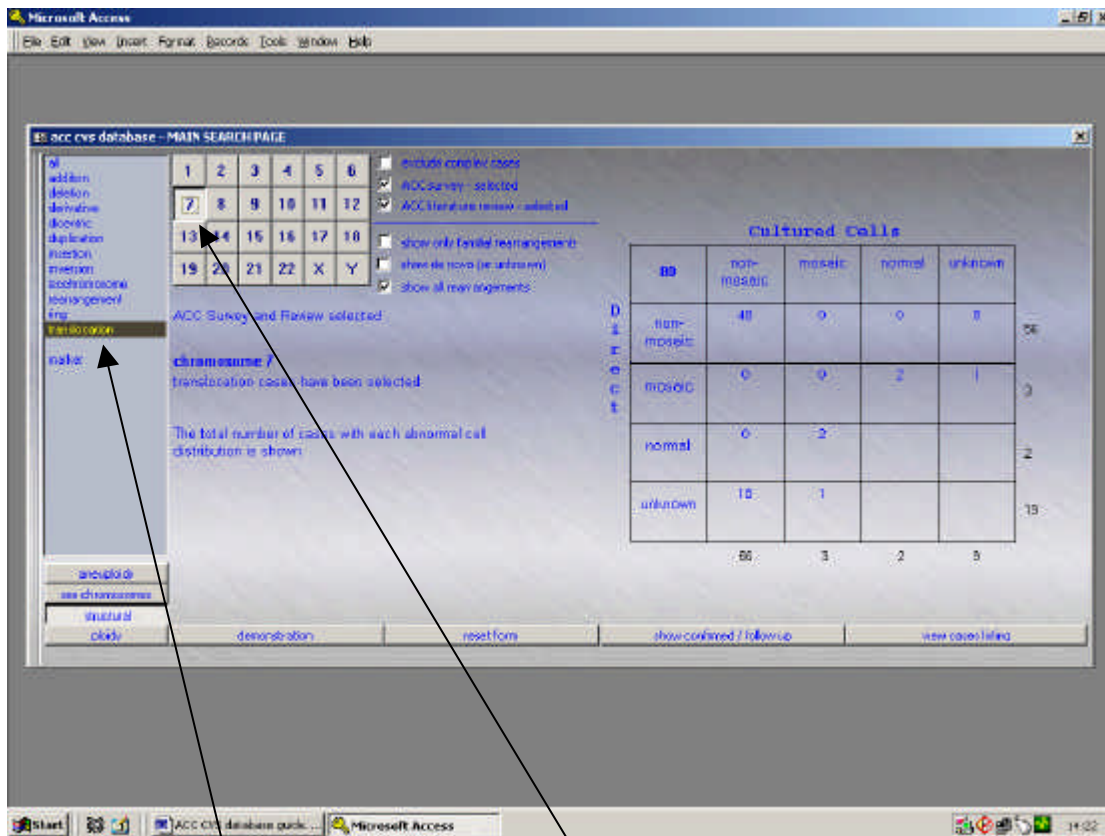
Bear in mind that you may need to search more than one abnormality type to get all the cases you need. It is possible to select more than one sex chromosome abnormality type at the same time, but this can produce double entries in the Summary Table and Case Listings.



Select 'structural' and you will see the above structural Abnormality Type menu. The default is 'all' structural abnormalities.

You will notice that when selecting for 'all' structural abnormalities, with no chromosome specified, the Summary Table apparently contains quite large numbers of cases. These are mostly duplicate entries, because things like a t(3;10) are coded as two translocations, one of 3 and one of 10, and get counted twice. You will find that most double counting and duplications in Case Listings will disappear as more specific searches are made, but the odd really complex case may still crop up more than once. You can use the 'check for duplicate cases' option on the Case Listing page, to look for these, but this is probably not necessary most of the time.

Searching for cases of interest is much the same as for other abnormalities. One main additional feature is available on the structural Abnormality Type menu. All structural abnormalities are coded so that they can be classified as 'known familial', 'de novo' or 'unknown'. Options are available to search only the 'known familial' or the 'de novo' + 'unknown' sub-groups. Dumping the 'unknowns' with the 'de novo' cases actually causes few difficulties with subsequent searches, as numbers are small. They also logically sort themselves out in the Summary Table into 'likely to be familial' (non-mosaic) and 'likely to be de novo' (mosaic) groups.



Try a search on translocations, picking chromosome 7, and using the options of excluding or concentrating on known familial cases.

There are two significant limitations of current codings for structural abnormalities. Balanced and unbalanced forms of rearrangements are classified together, and there is no differentiation between reciprocal and Robertsonian translocations. At present, the number of non-familial cases on the database is sufficiently small that this causes no problems. Sorting out the outcome of familial rearrangements is low priority in terms of this database aimed primarily at identifying CPM. These areas of coding will be looked at in future.